NaHCO₃ does not affect arterial O₂ tension but attenuates desaturation of hemoglobin in maximally exercising Thoroughbreds

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Manohar, Murli, Thomas E. Goetz, and Aslam S. Hassan. NaHCO₃ does not affect arterial O₂ tension but attenuates desaturation of hemoglobin in maximally exercising Thoroughbreds. J Appl Physiol 96: 1349–1356, 2004. First published December 12, 2003; 10.1152/japplphysiol.01083.2003.—The objective of the present study was to examine the effects of preexercise NaHCO₃ administration to induce metabolic alkalosis on the arterial oxygenation in racehorses performing maximal exercise. Two sets of experiments, intravenous physiological saline and NaHCO₃ (250 mg/kg iv), were carried out on 13 healthy, sound Thoroughbred horses in random order, 7 days apart. Blood-gas variables were examined at rest and during incremental exercise, leading to 120 s of galloping at 14 m/s on a 3.5% uphill grade, which elicited maximal heart rate and induced pulmonary hemorrhage in all horses in both treatments. NaHCO₃ administration caused alkalosis and hemodilution in standing horses, but arterial O₂ tension and hemoglobin-O₂ saturation were unaffected. Thus NaHCO₃ administration caused a reduction in arterial O₂ content at rest, although the arterial-to-mixed venous blood O₂ content gradient was unaffected. During maximal exercise in both treatments, arterial hypoxemia, desaturation, hypercapnia, acidosis, hyperthermia, and hemococoncentration developed. Although the extent of exercise-induced arterial hypoxemia was similar, there was an attenuation of the desaturation of arterial hemoglobin in the NaHCO₃-treated horses, which had higher arterial pH. Despite these observations, the arterial blood O₂ content of exercising horses was less in the NaHCO₃ experiments because of the hemodilution, and an attenuation of the exercise-induced expansion of the arterial-to-mixed venous blood O₂ content gradient was observed. It was concluded that preexercise NaHCO₃ administration does not affect the development and/or severity of arterial hypoxemia in Thoroughbreds performing short-term, high-intensity exercise.

exercise-induced arterial hypoxemia; blood-gas tensions; metabolic alkalosis; hemoglobin-O₂ saturation; arterial desaturation during exercise

SIMILAR TO HUMAN ATHLETES (5, 31), strenuously exercising Thoroughbred horses routinely experience arterial hypoxemia and desaturation of hemoglobin, which limit performance (19). Metabolic acidosis is also observed in strenuously exercising racehorses as blood lactate concentration increases dramatically (19). To mitigate the adverse effects of acidosis and gain a putative ergogenic effect, racehorses are frequently premedicated with NaHCO₃. However, despite considerable investigation (1, 6, 8–10, 12, 15, 17, 18, 20, 21, 33), consensus does not exist regarding the beneficial ergogenic effects of NaHCO₃ premedication in racehorses. Previous studies have largely been focused on changes in the jugular venous blood acid-base status during and postexercise (6, 8–10, 12, 17, 18, 21, 33), although muscle enzymes, substrates, and metabolites have also been studied (8, 9, 15, 33). There has been one report in Thoroughbred horses, wherein arterial blood-gas tensions were examined during strenuous exercise performed after NaHCO₃ administration (20). In this report (20), NaHCO₃ administration markedly exaggerated the exercise-induced arterial hypoxemia; mean arterial O₂ tension during exercise performed at 80 and 110% of the maximal whole body O₂ uptake (V˙O₂ max) in the NaHCO₃ experiments was 11.1 and 9.2 Torr, respectively, lower than that in the saline-treated horses (20). However, effects of an NaHCO₃-induced accentuation of the exercise-induced arterial hypoxemia on the hemoglobin-O₂ saturation were not examined. Furthermore, horses premedicated with NaHCO₃ had significantly lower arterial O₂ tension, even during exercise performed at 40 and 60% V˙O₂ max (20), which, in healthy, unmedicated Thoroughbred horses, is not attended by changes in arterial O₂ tension (19, 23–27). These observations in exercising horses premedicated with NaHCO₃ (20) are in contrast with findings in human subjects, in whom exercise-induced arterial hypoxemia is largely unaffected by preexercise administration of NaHCO₃, but the associated alkalosis helps limit the desaturation of arterial hemoglobin (28). Because an exaggeration of the exercise-induced arterial hypoxemia following NaHCO₃ administration to horses (20) may adversely affect O₂ supply and, in turn, performance (5, 19), the objective of the present study was to reevaluate the effects of preexercise NaHCO₃ administration on the arterial oxygenation in Thoroughbred horses performing short-term, high-intensity exercise.

MATERIALS AND METHODS

Horses. Experiments were carried out on 13 healthy, sound Thoroughbred horses (5 fillies, 8 geldings), 3–6 yr old, and weighing 450 ± 23 kg. They were housed in an air-conditioned building and were accustomed to being handled by people. The horses were maintained on alfalfa hay and oats with free access to water. The horses were dewormed periodically and were inoculated with tetanus toxoid and strangles vaccine. Our protocols and procedures were approved by the Institutional Animal Care and Use Committees.

Exercise training and work intensity eliciting maximal heart rate. After initial familiarization with walking, trotting, cantering, and galloping on the high-speed treadmill for 1 wk, all horses were exercise trained for 7 wk (22–27). Thereafter, separate trials were undertaken to determine the work intensity eliciting maximal heart rate and stress failure of pulmonary capillaries (39), leading to exercise-induced pulmonary hemorrhage (EIPH). Galloping at 14 m/s on a 3.5% uphill grade elicited maximal heart rate, induced EIPH in all horses (as demonstrated by the presence of fresh blood in the...
trachea on postexercise airway endoscopic examination; Refs. 16, 22, 36), and could not be sustained for >120 s, despite vigorous humane encouragement. Thus this workload was selected for further experimentation.

**Experimental design and protocol.** All horses were studied in the placebo [intravenous (IV) physiological saline] and the NaHCO₃ treatments, which were carried out in random order, 7 days apart. All experimentation was carried out at an ambient temperature of 20–21°C.

In the NaHCO₃ experiments, ~5 min after completion of baseline measurements (rest 1) on quietly standing horses, 5% NaHCO₃ solution (Abbott Laboratories, Deerfield, IL) was administered at 250 mg/kg via a previously positioned catheter in the left jugular vein. For individual horses, the volume of 5% NaHCO₃ solution varied from 1,955 to 2,492 ml. Thereafter, horses stood quietly on the treadmill for 15 min. Then blood-gas variables and plasma protein concentrations were determined (preexercise data). In the placebo study, after completion of baseline measurements, an equivalent volume (1,955–2,492 ml) of physiological saline was administered IV, and preexercise measurements were made at corresponding intervals in the NaHCO₃ treatment. The sequence of placebo and NaHCO₃ experiments was randomized, and 7 days were allowed between treatments on every horse.

On completion of preexercise measurements, exercise began on the high-speed treadmill set at a 3.5% uphill grade in the following manner. Beginning with a walk at 2 m/s for 120 s, the belt speed was raised in increments of 1 m/s every 60 s until the speed was 6 m/s. After the horses had trotted at 6 m/s for 60 s, speed was raised to 8 m/s for 60 s and then to 14 m/s. On completion of 120 s of galloping at 14 m/s on a 3.5% uphill grade, the speed was decreased first to 5 m/s (trot) for 60 s and then to 2 m/s. Horses walked at 2 m/s for 300 s before the treadmill was stopped. In this incremental exercise protocol, along with continuous core temperature measurement, simultaneous arterial and mixed venous blood samples were obtained for determining blood-gas variables at 55–60 s of trotting at 6 m/s; at 55–60 s of exercise at 8 m/s; at 30, 60, 90 and 120 s of maximal exertion; and at 120 s of walk at 2 m/s. Also, plasma protein and mixed venous blood lactate concentrations were determined at 60 s of exercise at 8 m/s, at 120 s of maximal exertion, and at 120 s of walk at 2 m/s.

In both treatments, using a flexible fiber-optic endoscope (Pentax Fiberscopes, Orangeburg, NY), nasopharynx, larynx, and trachea (up to the carina) were examined 45–50 min postexercise to detect the occurrence of EIPH (16, 22, 36).

**Experimental procedures.** On the day of the study, after local anesthesia in the 17th intercostal space, the abdominal aorta was catheterized percutaneously (23–27). Thereafter, using local infiltration of 2% lidocaine HCl, cardiac catheters (8 F) with tip manometer (Millar Instruments, Houston, TX), fluid-filled lumen, and a thermistor (Edward Laboratories, Santa Clara, CA) were advanced into the pulmonary artery via introducers inserted into the left jugular vein. The catheter locations were confirmed by monitoring the characteristic phasic blood pressure waveforms on an oscillograph (E for M, Lanexa, KS). These catheters permitted simultaneous sampling of the aortic and pulmonary arterial (mixed venous) blood, as well as continuous monitoring of the pulmonary arterial blood (core) temperature during the experiments. After catheter placement, horses stood quietly on the treadmill for at least 45–50 min before baseline measurements were initiated.

Because higher osmolality of the 5% NaHCO₃ solution [1,190 mol/kg H₂O vs. that of physiological saline (308 mol/kg H₂O)] causes water absorption into the vascular compartment, the associated alterations in plasma volume or hydration status were assessed by monitoring changes in the plasma protein concentration (2, 7, 25). Because the quantity of circulating plasma proteins is constant in healthy animals, acute changes in plasma protein concentration are indicative of the changes in the plasma volume or hydration status (2, 7, 25). Plasma protein concentration was determined by refractometry (7, 25), and the %change in plasma volume was calculated as [(PP₁/PP₂ − 1.0) × 100, where PP₁ and PP₂ are the initial and the test plasma protein concentrations, respectively (2, 7, 25)]. Blood-gas variables were determined by using a calibrated blood-gas analyzer and CO-oximeter (ABL520, Radiometer, Copenhagen, Denmark), and all blood-gas tensions and pH data were corrected to the simultaneously measured pulmonary artery blood temperature. Mixed venous blood lactate concentration was also determined (23, 25, 26), and %O₂ extraction was calculated as (arterial-to-mixed venous blood O₂ content gradient/arterial O₂ content) × 100.

**Data analysis.** The data were subjected to repeated-measures, split-plot design analysis of variance (SAS statistical software version 8.2, SAS Institute, Cary, NC), and the treatment comparisons were made by using the least squares significant difference method (35). Data for the placebo as well as the NaHCO₃ experiments were also individually subjected to analysis of variance followed by Newman-Keuls multiple-range test (35) to determine the significant effects of work intensity and duration within each treatment. For all statistical analyses, the level of significance was set at P < 0.05. The data are presented as means ± SE.

**RESULTS**

**Arterial bicarbonate concentration and pH.** See Fig. 1. The IV administration of NaHCO₃ was well tolerated by the horses. Preexercise arterial pH increased to 7.494 ± 0.004 (vs. 7.401 ± 0.003 pre-NaHCO₃ administration; P < 0.0001) as arterial bicarbonate concentration increased to 36.3 ± 0.3 mM. Submaximal exercise in either treatment was not attended by changes in arterial pH from respective preexercise values. However, acidosis developed during maximal exercise in both treatments as blood lactate concentration increased markedly (Fig. 2). Although the extent of the net drop in arterial pH from the beginning to the end of maximal exertion (change in pH = 0.306 ± 0.020 and 0.310 ± 0.018 in the placebo and NaHCO₃ experiments, respectively) was not different between treatments, the arterial pH was maintained at a higher value (P < 0.001) in the NaHCO₃ experiments. At 120 s of maximal exercise, the arterial pH values in the placebo and NaHCO₃ experiments were 7.099 ± 0.028 and 7.177 ± 0.021, respectively (P < 0.001).

**Plasma protein and hemoglobin concentrations.** See Fig. 3. Following IV NaHCO₃ administration to standing horses, plasma protein concentration decreased (P < 0.0001) as 14.6 ± 0.6% expansion of the plasma volume occurred. Concomitantly, hemoglobin concentration also decreased (P < 0.01) in the NaHCO₃-treated horses. Incremental exercise in both treatments caused progressive increments in these variables; however, values observed in the NaHCO₃ experiments remained less than in the placebo study, indicating that expansion of the plasma volume persisted during exertion. Plasma volume in the NaHCO₃ experiments exceeded that in the placebo study by 12.7 ± 0.9% at 60 s of exercise at 8 m/s and by 10.7 ± 1.4% at 120 s of maximal exercise. Arterial hemoglobin concentration approached 22.2 ± 0.3 and 21.1 ± 0.3 g/dl at 120 s of maximal exertion in the placebo and NaHCO₃ experiments, respectively (P < 0.01).

**Core temperature.** See Fig. 4. The incremental exercise protocol caused a similar, progressive rise in core temperature as exercise duration increased in both treatments. At 120 s of maximal exertion, core temperature had increased by 3.4 ±
Desaturation of arterial hemoglobin was also evident at 30 s of maximal exercise in both treatments, and, as exercise duration progressed to 120 s, the desaturation of arterial hemoglobin intensified (Fig. 5B). However, arterial hemoglobin-O₂ saturation was higher (P < 0.05) in the NaHCO₃ experiments. At 120 s of maximal exercise in the placebo and the NaHCO₃ experiments, arterial hemoglobin-O₂ saturation was 84.7 ± 1.7 and 86.8 ± 1.3%, respectively.

**Mixed venous blood O₂ tension and hemoglobin-O₂ saturation.** See Fig. 5. Following NaHCO₃ administration, preexercise mixed venous blood O₂ tension decreased, but hemoglobin-O₂ saturation remained unaffected. The incremental exercise protocol caused work intensity-related reductions in these variables in both treatments. From our data, O₂ tension required for half-maximal saturation of the blood could not be determined at rest or during maximal exercise. During submaximal exertion, at ~50% O₂ saturation of hemoglobin in the mixed venous blood, partial pressure of O₂ in individual horses was 2.5–4 Torr less in the NaHCO₃ treatment (vs. placebo). However, during maximal exercise, at 9–12.5% O₂ saturation of hemoglobin in the mixed venous blood, the partial pressure of O₂ in the NaHCO₃-treated horses was 1.0–1.5 Torr less than in the placebo treatment.

**Arterial CO₂ tension.** See Fig. 6. Preexercise values of arterial CO₂ tension increased (P < 0.05) following NaHCO₃ administration. Whereas submaximal exercise was attended by a reduction in arterial CO₂ tension, hypercapnia of a similar magnitude developed during maximal exercise in both treatments. At 120 s of maximal exercise in the placebo and the NaHCO₃ experiments, arterial CO₂ tension had reached 55.4 ± 1.9 and 56.8 ± 1.6 Torr, respectively. During recovery from high-intensity exercise, a dramatic hyperventilation ensued in both treatments, as demonstrated by the large reduction in arterial CO₂ tension.

**Arterial and mixed venous blood O₂ contents.** See Fig. 7. Hemodilution in the NaHCO₃ experiments (Fig. 3B) caused the preexercise arterial and mixed venous blood O₂ contents (16.0 ± 0.4 and 11.5 ± 0.4 ml O₂/dl blood, respectively) to be less than corresponding values in the placebo study (P < 0.01), but the arterial-to-mixed venous blood O₂ content gradient remained unaffected.
In both treatments, a significant ($P < 0.0001$) increment in arterial blood $O_2$ content was observed during exercise as hemoglobin concentration increased. However, because of the attenuated increment in hemoglobin concentration in the NaHCO$_3$-treated horses (Fig. 3B), the increment in arterial $O_2$ content was also attenuated ($P < 0.01$). At 120 s of maximal exertion, arterial blood $O_2$ content in the placebo and the NaHCO$_3$ treatments was 25.7 ± 0.4 and 24.5 ± 0.3 ml $O_2$/dl of blood, respectively ($P < 0.01$).

Work intensity-related changes in the mixed venous blood $O_2$ content, arterial-to-mixed venous blood $O_2$ content gradient, and $O_2$ extraction were observed in both treatments. However, the arterial-to-mixed venous blood $O_2$ content gradient of exercising horses in the NaHCO$_3$ experiments remained less than corresponding values in the placebo study ($P < 0.01$). At 120 s of maximal exercise, the arterial-to-mixed venous blood $O_2$ content gradient in the placebo and NaHCO$_3$ experiments was $23.3 ± 0.4$ and $22.2 ± 0.3$ ml $O_2$/dl of blood, respectively.

Airway endoscopy. All horses were observed to have experienced EIPH in both treatments.

DISCUSSION

Our observations in the placebo study regarding arterial hypoxemia, desaturation of hemoglobin, hypercapnia, acidosis, hyperthermia, increased plasma protein and hemoglobin concentrations, as well as increased $O_2$ extraction in horses performing short-term, high-intensity exercise (Figs. 1–7) mirrored data reported previously (23–27). Our primary objective in this study was to examine whether preexercise NaHCO$_3$ administration exaggerates the exercise-induced arterial hypoxemia as reported by Lloyd et al. (20) and thereby adversely affects the arterial hemoglobin-$O_2$ saturation and $O_2$ content in Thoroughbred horses performing strenuous exercise. In this context, the major findings of the present study were as follows. 1) Preexercise IV NaHCO$_3$ administration did not affect the arterial $O_2$ tension in healthy Thoroughbreds at rest, during submaximal exercise, or during short-term, high-intensity exercise (Fig. 5A), which elicited maximal heart rate and caused stress failure of pulmonary capillaries resulting in EIPH. Thus preexercise induction of metabolic alkalosis (Fig. 1) did not affect the development and/or severity of arterial hypoxemia in maximally exercising Thoroughbreds. Although these findings conflict with those of Lloyd et al. in horses premedicated with NaHCO$_3$, they are in agreement with data in human subjects (28) that preexercise NaHCO$_3$ administration does not affect arterial $O_2$ tension during exertion. 2) In agreement with data in human subjects (28), we also observed an attenuation of the desaturation of arterial hemoglobin during short-term, high-intensity exercise in Thoroughbreds premedicated with NaHCO$_3$ (Fig. 5B). 3) Despite these observations, however, the arterial blood $O_2$ content in the NaHCO$_3$ experiments decreased both preexercise as well as during exercise (Fig. 7). This was a consequence of the hemodilution that

Fig. 3. Concentrations of plasma protein (A) and hemoglobin (B) decreased following IV administration of NaHCO$_3$ to standing horses, indicating an expansion of plasma volume. With exercise, plasma protein and hemoglobin concentrations increased in both treatments; however, the values in the NaHCO$_3$ experiments were significantly less than in the placebo study, indicating that the expansion of plasma volume persisted during exertion. Values are means ± SE. *Statistically significant difference from correspondingly paired values in the placebo study ($A$: $P < 0.0001$; $B$: $P < 0.01$). †Statistically significant difference from all exercise data in the same treatment, $P < 0.0001$. ‡Statistically significant difference from rest #1 in the same treatment $P < 0.0001$. §Statistically significant difference from preexercise values in the same treatment, $P < 0.01$. ¶Statistically significant difference from 6 m/s in the same study, $P < 0.05$. ‰Statistically significant difference from 8 m/s in the same study, $P < 0.001$.

Fig. 4. Core temperature of horses increased progressively to similar values with increasing work intensity and duration in both treatments. Values are means ± SE. *Statistically significant difference from immediately preceding value in the same treatment, $P < 0.01$. 

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ensued following IV NaHCO₃ infusion (Fig. 3). 4) An attenuation of the exercise-induced expansion of the arterial-to-mixed venous blood O₂ content gradient occurred in the NaHCO₃ experiments (Fig. 7). In agreement with previous work (23–27), we observed in both treatments that arterial hypoxemia was well developed, even at 30 s of maximal exertion, and that further significant changes in arterial O₂ tension did not occur as exercise duration progressed to 120 s (Fig. 5). Recently, it was suggested that pulmonary injury (i.e., capillary stress failure)-induced airway inflammatory mediator release plays a role in bringing about the exercise-induced arterial hypoxemia (30, 31). All horses in the present study had experienced EIPH in both treatments, indicating that pulmonary capillary stress failure had occurred (39). According to the pulmonary injury-evoked inflammatory mediator release hypothesis (30, 31), an exaggeration of the arterial hypoxemia would be expected to occur with increasing exercise duration as structural changes in the blood-gas barrier (32, 39) intensify over time. Although this hypothesis has considerable appeal, the findings of Wetter et al. (40, 41) in exercising human subjects did not lend credence to it. Similarly, pretreatment of Thoroughbred horses with dexamethasone (to suppress the inflammatory response) and with a potent antihistaminic agent (H₁-receptor antagonist, tripelennamine HCl, to mitigate the effects of airway inflammatory and mast cell-released histamine on pulmonary capillary permeability) also did not support the pulmonary injury hypothesis for exercise-induced arterial hypoxemia in racehorses (26, 27). Furthermore, blood-gas studies during a repeat bout of strenuous exercise performed soon after the first exercise bout have also discounted the importance of structural changes in the blood-gas barrier (32, 39) in bringing about the exercise-induced arterial hypoxemia in human subjects as well as horses (4, 11, 23, 34). Among the causes of exercise-induced arterial hypoxemia in racehorses are the diffusion limitation to transfer of O₂ in the lungs (due to a significantly shortened pulmonary capillary transit time), the so-called relative alveolar hypventilation [as indicated by the
exercise-induced arterial hypercapnia (Fig. 6), despite significantly increased alveolar ventilation, and the ventilation-perfusion inequality (5, 19, 37). The contribution of relative alveolar hypoventilation to exercise-induced arterial hypoxemia would have been similar in our placebo and the NaHCO3 treatments, as indicated by the similarity of arterial CO2 tension during maximal exercise (Fig. 6). Although NaHCO3 administration caused CO2 retention in standing horses, arterial CO2 tension during maximal exercise was not different from values in the placebo study. It is known that, despite synchronization of respiratory and stride frequencies in galloping horses, minute ventilation is not mechanically limited, as significant increments in tidal volume have been demonstrated on increasing treadmill slope at constant speed (3) and with a reduction in inspired O2 concentration (29). This may account for the similarity of arterial CO2 tension in exercising horses in the placebo and the NaHCO3 treatments (Fig. 6).

Although in agreement with previous work (23–27), desaturation of arterial hemoglobin was observed during maximal exertion in both treatments (which intensified as exercise duration progressed to 120 s); an important finding in the present study was the significant attenuation of the desaturation of arterial hemoglobin in the NaHCO3 experiments (Fig. 5B). Because arterial O2 tension had not changed significantly in going from 30 to 120 s of maximal exercise in either treatment, it is likely that the intensification of the desaturation of arterial hemoglobin with increasing exercise duration was caused by the progressive rightward shift of the hemoglobin-O2 dissociation curve as hyperthermia (Fig. 4), acidosis (Fig. 1), and hypercapnia (Fig. 6) intensified over time. Although the extent of exercise-induced hyperthermia, acidosis, and arterial hypercapnia was similar in the two treatments, the fact is that arterial pH of the exercising horses in the NaHCO3 experiments was maintained at a significantly higher value (Fig. 1). The higher arterial pH of NaHCO3-treated horses during galloping at 14 m/s on a 3.5% uphill grade likely contributed to the observed attenuation of the desaturation of arterial hemoglobin by limiting the extent of rightward shift of the hemoglobin-O2 dissociation curve. Despite these findings, the fact is that the arterial blood O2 content of exercising horses in the NaHCO3 treatment was significantly less than that in the placebo study (Fig. 7). This was because of the significant hemodilution that ensued following IV administration of NaHCO3 (Fig. 3). Erythrocyte 2,3-diphosphoglycerate is another factor known to attenuate the desaturation of arterial hemoglobin by limiting the extent of rightward shift of the hemoglobin-O2 dissociation curve; however, differences in this variable between the placebo vs. NaHCO3 treatments were not examined in the present study.

In the NaHCO3-treated horses, a significant expansion of the plasma volume was demonstrated by the markedly diminished concentrations of plasma protein and hemoglobin (2, 7, 25), both preexercise as well as during exercise (Fig. 3). Although the hemodilution caused on NaHCO3 administration did not significantly affect the arterial-to-mixed venous blood O2 content gradient in standing horses, a significant (P < 0.01) attenuation of the exercise-induced expansion of the arterial-to-mixed venous blood O2 content gradient was observed (Fig. 7). Whole body O2 consumption is the product of cardiac output and arterial-to-mixed venous blood O2 content gradient (Fick principle). Thus, because NaHCO3 administration does not affect VO2 max (8, 20, 21, 28), it follows that the smaller arterial-to-mixed venous blood O2 content gradient of maximally exercising horses in the NaHCO3 experiments (Fig. 7) would have been attended by an augmented cardiac output. Preexercise hypervolemia-induced further significant increase in cardiac output has been demonstrated in maximally exercising horses (13) and human subjects (14, 38). In maximally exercising horses, a 16% augmentation of cardiac output followed preexercise ~20% expansion of the plasma volume (13). This discussion regarding a further augmentation of cardiac output of maximally exercising horses in the NaHCO3 treatment is relevant to the mechanism(s) for exercise-induced
arterial hypoxemia (Fig. 5) in that the largest contribution to exercise-induced arterial hypoxemia in racehorses is from the diffusion limitation to transfer of O₂ (37). The latter is probably related to the significant shortening of the transit time for blood in the pulmonary capillaries as cardiac output increases dramatically (5, 13, 19, 37). The scenario that maximally exercising horses in our NaHCO₃ experiments may have had augmented cardiac output (13), in turn, suggests that there would have been a further truncation of the already shortened pulmonary capillary transit time during high-intensity exercise, which may have adversely affected the arterial O₂ tension. Although this was not found to be the case in the present study (Fig. 5), our findings are in agreement with previous studies in human athletes (38, 42) and in racehorses (25), wherein pre-exercise hyperventilation also failed to significantly affect the exercise-induced arterial hypoxemia. It is plausible that hyperventilation induced following NaHCO₃ administration affected the pulmonary capillary blood volume and the distribution of ventilation-perfusion mismatching within the lungs, thereby affecting the pulmonary gas exchange of exercising horses.

Conflicting views have been presented regarding the ergogenic effects of preexercise NaHCO₃ administration to racehorses (1, 6, 8–10, 12, 15, 17, 18, 20, 21, 33). In our experiments, neither were the investigators blinded as to the treatments nor was run time to fatigue determined; therefore, an assessment could not be made in this regard. However, based on our perception of the effort and encouragement required for individual horses to complete the 120 s of galloping at 14 m/s on a 3.5% uphill grade, it is opined that the placebo and NaHCO₃ treatments were comparable.

In conclusion, our data demonstrated that preexercise IV administration of NaHCO₃ to cause metabolic alkalosis in healthy Thoroughbred horses did not affect the development and/or severity of arterial hypoxemia during short-term, high-intensity exercise that elicited maximal heart rate and caused stress failure of pulmonary capillaries, resulting in EIPH. However, a significant attenuation of the desaturation of arterial hemoglobin was observed during maximal exercise in the NaHCO₃-treated horses, which had higher arterial pH. Despite these observations, the arterial blood O₂ content of exercising horses was found to be less in the NaHCO₃ experiments because of the hemodilution, and a significant attenuation of the exercise-induced expansion of the arterial-to-mixed venous blood O₂ content gradient was observed.

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